REPORT OF CHRISTINE ALLEN

IN

IN RE PACIFIC FERTILITY CENTER LITIGATION

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TABLE OF CONTENTS

I. Professional Background and Qualifications

For almost 20 years, I have been an active embryologist, embryology researcher, and consultant. My experience ranges from operating as a clinical embryologist with expertise in freezing and thawing human embryos and oocytes, to research that led to the development of the Irvine Scientific Method of vitrification – now widely used in the IVF industry – to consultation work to audit IVF labs and help them attain quality outcomes. In addition to my work with numerous IVF clinics and labs, I have also published a number of scientific articles and abstract presentations in several peer reviewed scientific communication vehicles.

I initially entered the field in Brazil, as a trainee embryologist while earning my undergraduate degree in Biomedical Science. After completing my BS degree in 2001, I received PGD training at the Reproductive Genetics Institute in Chicago, Illinois. Upon returning to Brazil, I worked as an embryologist at the PUCRS IVF lab while simultaneously serving as an assistant professor in the medical and nursing schools at PUCRS university for the disciplines of embryology, advanced physiology, biochemistry, biomedical applied physics, and histology.

In 2002, I began pursuing a master's degree in Mammal Reproduction at UFRGS university in Brazil. My research focused on the vitrification of oocytes, a process which had not been successfully developed at that time. In 2003, I was selected to join the University of Michigan as a research assistant in a collaborative project with Irvine Scientific; my research there led to the first clinically proven technology for human oocyte cryopreservation accepted by the FDA and used worldwide. From 2004 through 2006, sponsored by Irvine Scientific, I traveled around the world training IVF clinical embryologists on how to perform the oocyte vitrification techniques I had developed. This experience provided me the opportunity to better understand different IVF settings and unique regional, legal, and technical problems in the industry around the world.

Concurrent with my training travels, I acted as a clinical embryologist in the IVF lab at the University of Michigan hospital. My regular duties there included fertilizing oocytes, culturing embryos, and vitrifying and warming oocytes and embryos, among other things. In April 2006, I joined IVF Michigan as the Technical Supervisor of the Ann Arbor location of Michigan's largest IVF clinic. My regular duties there included clinical embryology work, andrology coordination, troubleshooting within the IVF laboratory, proficiency testing of lab staff, and quality control within the lab.

In 2010, I began working as an embryologist in the IVF lab at Wayne State University, and, also during that period, I started a master's degree course at Eastern Virginia Medical School, the only university in the world to offer a master's degree in clinical embryology at the time. I earned my master's degree in that field from EVMS in May 2013. I later completed a doctorate in Toxicology with the UFSM university in Brazil via remote attendance.

Upon earning my master's in clinical embryology in 2013, I started a consulting business

specializing in IVF laboratory technologies and expert personnel – Elite IVF. As the Clinical Director of Elite IVF, I oversee a team that supervises ART laboratories regarding their performance of quality control procedures, sample testing, andrology testing, embryology procedures including micromanipulation, cryopreservation and PGD, billing procedures, purchasing management, professional assistance, medical and laboratory training, plan and overview of hormonal stimulations and advise to outside clinicians on interpretation of results. I also analyze clinic and laboratory statistics. Elite IVF also provides per diem staff for embryology, andrology, genetics counseling and anesthesiology. On average, my team sees an increase in pregnancy rates from 15% up to 75% in client projects. One unique service I personally provide through Elite IVF is education and guidance of IVF clients, when referred by their physicians, to analyze failed IVF cases and suggest possible improvements to achieve pregnancy.

In addition to my work with Elite IVF, I served as the Technical Laboratory Director of California Cryobank in Los Angeles, California from 2015 to 2017. I have also worked as a laboratory director, scientific director and/or laboratory operations director of several IVF clinics, in Mexico, Brazil, the U.S., and Thailand, and I have troubleshot and implemented new technologies in over 80 IVF clinics.

I am also an active member of the American Society of Reproductive Medicine (ASRM), serving on the board for scientific review in my area of expertise. And I am one of the elected Chairs at the American Board of Bioanalysis (ABB), representing the College of Reproductive Biology (CRB).

I hold two TS (technical supervisor) certifications issued by the American Board of Bioanalysis, for the disciplines of andrology and embryology, and I have earned a Clinical Laboratory Scientist (CLS) license in the state of Louisiana.

In addition to IVF clinical work, I currently serve as an active expert advisor for Guidepoint, a consultant firm that provides expert consultations for capital venture investors, and I also serve on the development board of Fleury Hospitals-Sao Paulo- Brazil, in the IVF laboratory development. I am currently also serving as Consultant Chief Scientific Officer for Healthpoint Venture Capital US regarding its IVF portfolio.

My curriculum vitae is attached as Exhibit 1.

II. Engagement Regarding the Pacific Fertility Center (PFC) Tank 4 Incident

I was engaged by Plaintiffs' counsel in this action in June 2018 on behalf of IVF clients whose oocytes and embryos were stored at PFC in a cryogenic storage tank labeled "Tank 4" on March 4, 2018. On that date, laboratory staff at PFC discovered that Tank 4 had suffered a vacuum failure and loss of liquid nitrogen, resulting in the exposure of the tank's contents to a higher temperature than appropriate and uncontrolled thaw conditions (the "Tank 4 incident").

I was retained to provide my professional opinion concerning the incident and its impact on Plaintiffs, and to provide background about the IVF process. This is a preliminary report, as discovery is ongoing, and I expect to supplement my opinions as additional information is made available through that process.

I have not previously testified in a court case. My rates in this matter are $200/hour for consulting and $400/hour for testifying.

III. Analysis

A. A Brief Explanation of Embryology

Embryology is a biomedical discipline field, derived from the broad studies of eukaryotic developmental biology. The embryology field of science and medicine is responsible for the understanding of all developmental phases of unborn beings, including humans, from prenatal development of gametes (reproductive cells), fertilization process, and further development of embryos and differentiation of embryonic tissues into fetuses. In addition, a specific segment of embryology, known as teratology, addresses congenital disorders, derived from environmentally caused or parental inherited genetic origin.

B. The In Vitro Fertilization (IVF) Process

IVF is a form of Assisted Reproductive Technology (ART). It is a common fertility treatment for individuals who are unable to conceive naturally for more than one year of attempting to achieve pregnancy and for individuals seeking to preserve their fertility options for a future pregnancy. While common, IVF is also physically invasive, financially costly, and emotionally taxing. It consists of over-stimulating the maturation of several oocyte-containing ovarian follicles by administration of reproductive hormones and surgically collecting a cohort of a female's oocytes (eggs). The oocytes can then either be cryopreserved and stored for later use or fertilized in an embryology laboratory to create embryos. Embryos created by this process can either be transferred into the uterus in an attempt to achieve pregnancy or cryopreserved and stored for future use.

IVF starts with controlled ovarian stimulation (COS), which stimulates the ovaries to produce multiple mature oocytes (eggs) in a single reproductive cycle. In order to do this, a reproductive endocrinologist (that is, an REI) administers mammalian reproductive hormones, also called fertility drugs, via injection to the IVF client. This stimulates ovarian follicles containing immature oocytes to grow and mature. During this treatment, the individual's hormone levels and ovarian development should be closely monitored and tailored to safely achieve the best outcomes.

Once the ovarian follicles have grown to an appropriate size, an additional hormone injection is administered to trigger the final maturation of all oocytes, mimicking a natural LH surge in the female body. After that, oocytes at the Metaphase II stage of the meiosis

division (that is, mature eggs) can be surgically retrieved by ultrasound-guided transvaginal laparoscopy and transported to the IVF lab. Oocyte retrieval, or egg retrieval, is performed with the individual under sedation by an intravenous (IV) sedative-hypnotic agent in addition to prophylactic antibiotic treatment and IV aspirin.

In the meantime, and separate from the oocyte retrieval, a semen sample is collected from the IVF client's reproductive partner or a semen sample from a donor is thawed. An andrologist examines the sperm and separates the sperm to be used for fertilization from the semen.

Once both sets of gametes (the eggs and sperm) are recovered, an embryologist fertilizes the eggs. Conventional insemination of oocytes is achieved by simply adding sperm to oocytes in a petri dish. Alternatively, the embryologist may employ the micro-surgical process of intracytoplasmic sperm injection (known as ICSI), manually injecting a sperm cell into each mature oocyte. Whichever method is used, the fertilized eggs are kept in a petri dish containing a culture medium that mimics human tubal fluids and placed into an embryology incubator with strictly controlled temperature and humidity for 18 hours. Exactly eighteen hours after insemination, an embryologist checks if any of the oocytes have been normally fertilized by confirming the presence of two pronuclei in the cytoplasm of each egg. Once an egg shows two pronuclei (commonly referred to as 2PN), with one containing maternal and the other containing paternal genetic material, it is called a zygote. Zygotes are transferred to a culture medium comparable to uterine fluids, and embryologists continue to monitor their development for five to six days. Only those zygotes that develop into blastocysts, meaning an embryo that has achieved the first level of differentiation with two cell lines, can be either transferred into the IVF client's uterus or cryopreserved and stored for future use.

To be viable, however, an embryo must be of good quality, and it is important to note that not every zygote evolves into a viable embryo. An embryo is categorized as good quality when it presents a grown, well differentiated inner mass cell (IMC) inside a pocket of outer cells (the trophectoderm, which will become the placenta and gestational membranes). Poor quality embryos, i.e., embryos that are severely developmentally delayed, present a high amount of cellular fragmentation debris, or are completely developmentally arrested, are not suitable for transfer and are, by default, considered non-viable embryos.

In many cases of IVF, the fertilization process creates more than one embryo. A multiplicity of embryos increases the chances of pregnancy by providing the clinical embryology professionals the opportunity to choose the embryo with the best morphological characteristics and appropriate developmental timing to be transferred into the uterus. Being able to choose among multiple embryos allows embryology professionals to mitigate for factors that affect embryo formation and development, such as the genetic makeup of the gametes (oocyte and sperm), the type and length of hormonal stimulation for the IVF client, and the intrinsic embryonic response to environmental factors in the embryo culture, among others.

Once viable embryos have been created through the IVF process, the embryos can be immediately transferred into a uterus, cryopreserved and stored for later use, or biopsied for genetic testing (to identify gender and any chromosomal defects) and then cryopreserved for use depending on the test results. The second option, to cryopreserve and store the embryos for later use, is commonly advertised by IVF clinics as an option for people not currently seeking a pregnancy to preserve their fertility options.

When an IVF client is planning to transfer an embryo created through the IVF process, she must undergo a second phase of hormonal replacement treatment (separate from the hormonal treatment required for egg retrieval). This hormone treatment readies the uterus of the IVF client to receive an embryo and maintain a pregnancy. One blastocyst-stage embryo per cycle is typically transferred directly into the uterus, via vaginal-uterine cervical catheter insertion. More than one embryo can be transferred to increase the chance of pregnancy. However, transferring multiple embryos also increases the chance of multiple gestation (e.g., carrying twins), along with the medical risks associated with multiple gestation and delivery.

Once an embryo is transferred into the uterus, a blood test is completed approximately nine days later. If the blood test detects the presence of the hormone hCG, it signifies that the transferred embryo has implanted in the uterus. Another blood test is done approximately one week later. A significant increase in hCG in the second sample indicates a viable pregnancy. At least two transvaginal ultrasounds are then performed, with a two week interval between them, to determine the presence of an intrauterine gestational sac with a viable conceptus that presents normal measurements for its gestational age. The ultrasounds will also show whether the fetus presents a normal early life heartbeat rate.

If any of these tests indicates that the pregnancy is not viable, or that it has been spontaneously terminated, the IVF client may choose to undertake another IVF cycle or to use her/his cryopreserved embryos.

C. Cryopreservation Methods

The modern method for cryopreserving biological material is vitrification, which is a form of ultra-rapid cooling that utilizes high concentrations of cryo-additives. Vitrification brings the material being cryopreserved to an amorphous state with kinetic characteristics equivalent to a solid, without forming ice crystals or suffering the transformations of molecular solidification, both of which are a major cause of intracellular cryo-damage. The vitrified sample contains the normal molecular and ionic distributions of the original liquid state and can be considered an extremely viscous, supercooled liquid. In this technique, oocytes or embryos are slightly dehydrated by rapid exposure to a concentrated solution of cryoprotectant and cryo-additive before plunging the samples directly into liquid nitrogen. The use of vitrification offers an important advantage in protecting genetic material, because, in contrast to slow-rate

freezing, it does not permanently disrupt metaphasic spindles, nuclear chromosomes, or intracellular membranes.

The goal of vitrification in IVF is to cryopreserve the oocytes and embryos in a vitreous state, with as little ice formation as possible. This is because a vitreous solution is an amorphous solid-like liquid that induces no segregation – and thus no physical or osmotic damage - within the cellular physiologic apparatus of the sample being vitrified, while freezing does cause segregation. To create a vitreous solution rather than ice crystal formation in the vitrification process can be challenging because it requires maintaining a sufficiently high cooling rate. A higher cooling rate will result in vitreous solution, while a lower cooling rate will result in water segregation and ice crystal formation.

Vitrification is a highly technical process that requires a well-trained embryologist to perform both the vitrification and the subsequent thaw. (6) The length of time the sample is exposed to cryoprotectants and the liquid nitrogen used during both cooling and thawing must be extremely precise. Exposure to the cryoprotectants, in particular, must be carefully controlled because, at room temperature, they are effectively toxins. For instance, one of the cryo-additives required for consistent success when vitrifying reproductive material is dimethyl sulfoxide (known as DMSO) (8,9) - a neurodevelopmental cytotoxic chemical organosulfur compound (9) The cooling rate during vitrification and the warming rate during thaw must be carefully controlled because an improper cooling or warming rate will allow ice crystals to form in – and damage – the cells. In fact, the avoidance of ice crystal formation during the thawing procedure may even be more important than during the initial vitrification. This is because when warming the sample from -196ºC to room temperature, the passage through -137 ºC and 0ºC (when ice crystals form, expand, melt and water reenters the cells) is inevitable at atmospheric pressure conditions. Thawing technique must be performed by highly trained cryo-technologists, with the understanding that velocity and precision of micromanipulation determine for how long the formed ice crystals will grow, potentially damaging internal cellular structures. Nonetheless, vitrification can result in the survival of 100% of the cells in a cryopreserved sample and yields high viability rates for thawed material. (6)

Vitrification replaced the slow-rate freezing method commonly used in IVF prior to the mid-2000s. As the name implies, this alternative method utilized a slower rate of cooling than vitrification. It also relied on severely dehydrating the sample to be cryopreserved. While the slow-rate freezing method is much simpler to perform than vitrification, requiring virtually no technical skills, it leads to cell damage in more than 50% of cells subject to the method and generally yielded viability rates post-thaw that are 45% lower than those yielded for vitrified material. Slow-rate freezing has been completely discontinued in the vast majority of IVF clinics around the world due to its poor performance. (5,6)

Regardless of the cryopreservation method used, any cryopreserved specimen will suffer irreversible damage due to ice crystallization when exposed to surrounding temperatures between -150ºC and -132°C, which is the glass transition point of water, when nucleation of ice starts taking place. Small sized specimens are at the greater risk of complete loss due to their

low thermal mass (size), which makes them more susceptible to adaptation to the extracellular temperature. In addition, oocytes are the largest cell of a mammal organism, presenting a much larger volume in comparison to any other cell, including embryonic cells. Its large cellular volume makes oocyte cryopreservation the biggest challenge in human tissue cryopreservation, as the necessary surface-to-core even dehydration and fast cooling rate for avoidance of ice crystal formation during cryopreservation are much harder to achieve. Therefore, the risk of intracellular ice crystal formation during short exposure to warmer temperatures, causing intracellular damage, is greater for oocytes than embryos, though both are at risk with temperatures warmer than -150ºC. When samples reach temperatures above -132º C, the formation of ice crystals reaches its most-likely crystallization point for the cryopreservation solutions used in vitrification of oocytes and embryos. Vitrified biological samples are expected to be damaged by the mechanical disruption of cell membranes caused by ice crystal formation from that temperature point and up. [7]

D. Equipment Used in IVF

The IVF and embryology laboratory is by necessity an especially clean environment, with dedicated air filtration systems for the room and horizontal laminar flow hoods forcing filtered air over the microscopes used to handle materials to avoid contaminated air reaching gametes and embryos.[3] IVF conditions require temperature-controlled surfaces on all microscopes and manipulation areas. If temperatures are not precisely maintained, and the reproductive material is exposed to any level of temperature warmer than -150º C, the vitreous state of cryopreserved samples is compromised and samples are likely to be damaged or completely destroyed due to the ice crystallization of the aqueous content of the cells. From a thermophysics point of view, this crystallization may start occurring at -150º C, and optimum ice crystal formation (when the most damage occurs) takes place right above -132º C (the vitreous to ice transition point of water). [1]

ICSI, laser assisted hatching, and embryonic biopsy require micromanipulation via a manually controlled and calibrated ultra-precise robotic system that is required for all IVF treatments. The developing gametes and embryos are maintained in precisely controlled and maintained incubators, fed with a mix of gases which replicate the environment of the fallopian tubes. Controls for temperature, humidity, biological and toxic contamination, and concentration of gases must be precise in all embryology incubators.

i. Tanks

Although utilization of techniques properly based in thermodynamic principles along with precise performance of vitrification and warming are imperative for successful preservation of reproductive cells and embryos, proper maintenance of their vitreous state is equally important. The maintenance of temperatures below -150ºC is necessary to preserve any sample imbedded in cryoprotectants, such as DMSO.

The stable low temperatures needed in the cryostorage vessel are secured by using cryogenic tanks designed and manufactured to sustain such low temperature with reliability

and durability. Cryogenic tanks, also called cryotanks, or, specifically in the embryology field, IVF tanks, consist of stainless-steel vessels, similar to a giant thermos carafe, that are used to store cryopreserved biological material at very low temperatures. These cryogenic tanks store materials at temperatures colder than -150^{o} C [1,2, 3].

The ultra-cold temperatures maintained in cryogenic tanks by the vacuum jacket are achieved by the use of ultra-cold gas elements, in their liquid phase. Examples of gases that become ultra-cold when submitted to pressure, acquiring liquid properties, are oxygen, hydrogen, argon, natural gas, helium and nitrogen. Each gas, when in its liquid form, acquires a constant just-below evaporation temperature, which is maintained inside the cryogenic vessel. In IVF and embryology labs, liquid nitrogen is used to maintain cryopreserved gametes and embryos at -196^{o} C while the samples are fully submerged in the liquid nitrogen inside cryogenic tanks. [1,2]

There are several models of cryogenic tanks used for biological storage. Tanks may vary in size, shape, shape of inner carrousels for sample organization, capacity, mobility, durability, insulation capacity, and metallurgic materials used to construct these vessels. In the IVF field, cryogenic tanks are usually constructed of durable stainless steel, of large capacity (above 1000L), and with multi-layer insulation (including a vacuum layer).

ii. Controllers

Cryogenic tanks that are storing cryopreserved material must be monitored for temperature maintenance and liquid nitrogen level. [3] Liquid nitrogen level monitoring can be done manually, using a dipstick to measure the liquid nitrogen level inside the tank, but is usually done via an electronic controller, with manual checks done daily to validate the controller reading accuracy. Electronic controllers also provide temperature readings and monitoring via probes placed at both the top and the bottom of the samples inside the tank. Electronic controllers are set to emit audible alarms and can initiate warning phone calls via a call device when the temperature or nitrogen levels deviate from user-set parameters. When tanks are connected to a separate and substantial liquid nitrogen supply, as are most tanks over 500L capacity, electronic controllers can also be set to automatically refill the liquid nitrogen. [3]

iii. Tank and Controller Operation and Maintenance

Laboratory managers and staff can and should take several measures to protect themselves while operating cryogenic tanks and to protect cryopreserved material in storage. To safely operate cryogenic tanks, for instance, all personnel who use and come in contact with the tanks or liquid nitrogen must be trained to use the tanks and interact with the cryopreserved samples. Safety precautions should be taken at all times, and appropriate protective gear should be worn, such as goggles, helmets, gloves and overalls.

In the specific case of reproductive samples, maintaining the proper level of liquid nitrogen in the cryogenic storage tanks is vital for the safety of the material. Clinics must have

systems and processes in place to ensure tanks and controllers are monitored and properly handled. These systems and processes should include daily tank inspections, the use of electronic controllers as standard practice to monitor tank temperature and liquid nitrogen levels and usage and to autofill liquid nitrogen as needed, and alarm systems that both audibly alert anyone present in the lab and call out to staff when monitored parameters are out of range. The systems and processes should include regular review of lab equipment with prompt repair or replacement when problems are identified.

E. IVF Success Rates

i. Statistical Reporting of Success Rates

Success rates for IVF cycles may be interpreted in several ways. Several benchmarks for success rates are used to define clinical success of a cycle, starting with an initial positive hCG blood test, which indicates that a pregnancy has been initiated by attachment of an embryo in the uterus. A viable pregnancy is confirmed by a transvaginal ultrasound that shows the pregnancy is intrauterine (inside the uterus), and not ectopic (embryo implantation in a place other than the uterus). A positive ultrasound exam will also confirm the presence of a gestational sac with a fetus inside it and present the sound of a healthy fetal heartbeat. If all four datapoints (positive hCG, intrauterine presence of gestational sac, sac with normal conceptus, and presence of a heartbeat) fall within normal ranges for pregnancy, the IVF client is reported to have achieved a clinical pregnancy.

The ultimate and most important benchmark for success in an IVF cycle, however, is the delivery rate. Since a significant percentage of clinical pregnancies may end in spontaneous miscarriages, a percentage that escalates with maternal age due to genetic abnormalities in the aging oocytes, the percentage of live births is considered the most important indicator of success of an IVF cycle, from the clinical, medical, and psychological points of view. It has been demonstrated that IVF-born babies have comparable rates of birth defects, stillbirths, and genetic diseases, with only a slight increase of a few rare genetic disorders, and increased epigenetic changes, in comparison with naturally conceived children. (10)

From a laboratory quality control point of view, keeping track of the number of mature oocytes retrieved, in comparison to overall oocytes retrieved, the number of zygotes developed per total inseminated eggs, and the number of blastocysts developed from the total number of zygotes are all common metrics used to determine if a specific case deviates from the mean benchmarks accepted by a given laboratory. Overall percentages of these benchmarks are used as a simple way to produce a statistical bell curve and determine if a certain period of time or a certain individual result is within less than one or two standard deviations of what is expected for that laboratory. (10)

IVF clinics in the U.S. have been required to register themselves as IVF practitioners and report their success rates to the CDC since 1992. (11) In addition, in the past few years, the ASRM has created a paid-to-report database for its members. (11) This database employs

standardized definitions of success for all clinics, such as successful pregnancies per each category of cycle started, and per age group. All information about each IVF client cycle is uploaded by the clinic and a report is created for public reference. Clinics that are in good standing and compliant with College of American Pathologists (CAP) standards (or a similar organization) must also report their treatment data to CDC, either directly or via the Society for Assisted Reproductive Technology (SART). Data reported to SART must be reviewed by the reporting clinic's medical director, who verifies the authenticity of the information provided.

ii. The Success Rates for Material Stored in Tank 4 are Lower than Expected

As compared against publicly available data, all individuals whose reproductive oocytes or embryos were stored at PFC in Tank 4 on March 4th, 2018 have been affected by the exposure of their oocytes and embryos to adverse conditions. PFC reports its success rates to SART and publishes those rates on its website as a client resource for research. PFC's data as reported to SART shows that the clinic's typical thaw success rate for embryos prior to the Tank 4 incident was between 97% and 100%. However, the successful thaw rate for embryos at PFC from Tank 4 since the incident are considerably below that range, at [redacted]

The typical thaw success rate for oocytes, based on scientific peer reviewed published data, is well above 90%. (13, 14, 15) Although I have not received sufficient information at this time to determine success rates of oocyte thaws at PFC prior to the Tank 4 incident, marketing materials for the clinic suggest that the PFC laboratory performs as a leader in the IVF field and exceeds national average expectations. The successful thaw rate for oocytes that were stored in Tank 4 at the time of the incident, however, is only [redacted] This success rate is significantly lower than the 90% survival rate expected according to published scientific papers and leaders in the industry. To provide perspective, on average, a lab can expect that about 10% of cryopreserved oocytes will not survive being thawed. But for Tank 4 ooyctes thawed since March 4, [redacted] of those oocytes failed to survive thaw. When we compare pregnancy rates originated from vitrified oocytes, expected to be around 50% per set of 6 thawed oocytes, according to donor egg banking industry, the drop of pregnancy success for tank 4 may reach close to a [redacted] in expected delivery rates.

Based on SART data, the typical national confirmed pregnancy rate, meaning instances with a doubling hCG blood test and detection of a heartbeat, ranges from 49% to 56% in the maternal age bracket of greater than 35 to 40 years old. Prior to the Tank 4 incident, PFC reported an overall pregnancy rate, based on these same parameters, of 59%. However, PFC's confirmed pregnancy rate for Tank 4 material since the Tank 4 incident is significantly lower at only [redacted]

Based on SART data, the typical national confirmed live birth rate ranges from 36% to 43% for the maternal age bracket of greater than 35 to 40 years old. Prior to the Tank 4 incident, PFC reported an overall live birth rate ranging from 40.7% to 48.8% for that same maternal age group. However, PFC's live birth rate for Tank 4 material since the Tank 4 incident is much lower at only [redacted] according to documents provided to-date. In addition to this lower

live birth rate, it is unknown whether babies born from material that was in Tank 4 at the time of the Tank 4 incident will suffer negative health consequences as a result of exposure during that incident.

I've analyzed the reported success rates for Tank 4 material through September 2019, and they compare unfavorably to the expected success rates. In fact, several concerns are raised from the exposure to adverse conditions and potential developmental neurotoxicant exposure during the unfortunate Tank 4 incident. The low success rates revealed by PFC's data for Tank 4 material raise concerns not only about the low viability outcomes, but also about the quality of the material transferred. The lower rates of survival confirm exposure to adverse environmental conditions and an uncontrolled thaw. Where Tank 4 material has been transferred and resulted in live births, the final effects of the damage sustained by the samples is not yet known. As Dr. Herbert acknowledged during his deposition, there is no information in the scientific or medical literature about what clinical or developmental consequences may arise from proceeding with intrauterine transfer of such material: "Can you imagine the experiment where you thaw a human embryo uncontrollably and then try to make a baby out of it? I don't think so." As an embryologist, this raises great concerns to me about the decision to transfer embryos and embryos formed from oocytes stored in Tank 4 that were affected by the Tank 4 incident.

IV. Materials Reviewed

- SART data published at www.SART.org
- CDC data published at www.CDC/ART.org
- August 27, 2018 Response by ASRM to Plaintiffs' Subpoena for Production of Documents, including responsive documents
- August 30, 2019 Pacific MSO's Response to Plaintiffs' First Set of Interrogatories
- 09/10/19 Deposition of Pacific MSO and Alden Romney
- 10/01/19 Deposition of Dr. Carl Herbert
- 10/08/19 Deposition of Catrin Best
- 10/09/19 Deposition of Pacific MSO and Joseph Conaghan
- CHART000058-60
- CHART000088 (tank drawing)
- CHART000106 (tank drawing)
- CHART00918-1050 (technical manual)
- CHART002487 (tank drawing)
- CHART009515-9557 (catalog)
- MSO 011711 (email communications)
- MSO011553 (email communications)
- MSO000006-47 (Management Services Agreement)
- MSO000048-55 (Initial Embryo Storage Management Services Agreement)
- MSO000056-64 (Tissue Storage Management Services Agreement)
- MSO000065-79 (Photos of Tank 4)

- MSO0000080-309 (March 23, 2018 PFC Response to CAP Request for Information with all exhibits)
- MSO00310-363 (Reflections Data)
- MSO007390-7397 (March 23, 2018 Conaghan Letter to CAP)
- MSO01982-2220 (March 23, 2018 Letter from Joseph Conaghan to Dr. Desiree Carlson with exhibits))
- MSO021089-21250 (Technical Freezer Manual)
- MSO022465-67 (Tank 4 data)
- MSO025536-25596 (SART data)
- MSO025597-25600 (Tank 4 data)
- MSO021651 (email communications)
- MSO021654 (email communications)
- PRELUDE000369-377 (Tissue Storage Management Services Agreement)
- PRELUDE000427-434 (Initial Embryo Storage Management Services Agreement)
- PRELUDE002283 (March 8, 2018 email chain)
- PRELUDE002283 (email communications)

Dated 10/15/2019

Christine Allen

References:

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(2) Industrial gases handling. https://www.praxairdirect.com/Industrial-Gas-and-Welding-Information-Center/Safety/Cryogenic-Tank-Safety.html

(3) 'Quality and Risk Management in the IVF Laboratory': http://www.cambridge.org/

(4) Vitrification versus Slow Freeze gives excellent survival https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2729856/

(5) Developmental consequences of cryopreservation of mammal oocytes and embryos. https://www.rbmojournal.com/article/S1472-6483(10)62126-8/pdf

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(7) DMSO SDS https://www.fishersci.com/store/msds?partNumber=D1391&productDescription=DIMETHYL+SULFOXIDE+GC+HS+1L&vendorId=VN00033897&countryCode=US&language=en

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(9) ESHRE ART guidelines. https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Revised-guidelines-for-good-practice-in-IVF-laboratories-(2015).aspx

(10) CDC: https://www.cdc.gov/art/index.html

(11) SART: https://www.sart.org

(12) https://www.sciencedirect.com/science/article/abs/pii/S1472648310610723

(13) Vitrification: an effective new approach to oocyte banking and fertility preservation in cancer patients. https://www.researchgate.net/publication/226659970_Vitrification_An_effective_new_approach_to_oocyte_banking_and_preserving_fertility_in_cancer_patients

(14) Excmed Presentation: Inside ovary, oocyte and beyond: keys for success on cryopresrevation: https://www.excemed.org/sites/default/files/l12_cobo.pdf

EXHIBIT 1

Christine S. Allen M.S., TS

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EXPERIENCE

Elite IVF **Ann Arbor – MI** **11/2013 - present**

Clinical Director
Chief Scientific Officer

Implement troubleshooting technology, guarantee improvement on pregnancy rates and supervise ART laboratory including performance of all quality control procedures, sample testing, andrology testing, embryology procedures including micromanipulation, cryopreservation and PGD, billing procedures , purchasing management, professional assistance, medical and laboratorial training, plan and overview of hormonal stimulations and advise to outside clinicians on interpretation of results. Direct statistics and study designs to designees. Provide per diem staff for embryology, andrology, genetics counseling and anesthesiology. Legal expert witness consultants for tier 1 law firms in multiple cases involving IVF failures, IVF malpractice and negligency.

Achievements: Average increase in pregnancy rates from 15% up to 75% in client projects.

GUIDEPOINT Consultancy Firm **New York- NY** **12/01/2017 - present**

IVF and Cryobanking Expert Advisor

- **Provide availability for client phone consultations, data analysis, workshops for events related to client area of focus and specific needs.**

EVMS Eastern Virginia Medical School **Norfolk VA** **11/2017 - present**

Invited Assistant Lecturer

- **Provide specialized classwork and workshops for Embryology and Andrology graduate courses (MS/ PhD)**

ASRM Abstract Review Committee **05/2018 - present**

Evaluate and approve ASRM scientific abstracts for Annual meetings presentations.

American Board of Bioanalists - Committee of Reproductive Bioanalists 2019- 2022
Elected Chair of Continuing Education Credentials

STORK ART ASIA Bangkok, Thailand 03/2018-8/2018

Director of Laboratory Operations

- **Develop, implement, test and supervise high performance procedures and policies for ART laboratories;**
- **Lead laboratory accreditation process, subsequently maintaining it;**
- **Oversee performance of all quality control procedures, sample testing, andrology testing, embryology procedures;**
- **Maintain QC interactive policies for performance improvement, including micromanipulation, cryopreservation and PGS;**
- **Develop multi-center purchasing management, professional assistance, medical and laboratorial training, plan and overview of hormonal stimulation procedures;**
- **Provide clinical consultation to outside clinicians on interpretation of results.**
- **Perform monthly statistical analysis of performance and implement improvement modifications based on data collected;**
- **Develop and perform 3 step validation process for every change in technical aspects, assuring best practices, patient protection and best quality of IVF services in every modification necessary;**
- **Provide team's scientific knowledge updates;**
- **Elaborate research study designs, apply, collect and analyze data, and prepare submission for publications.**

Summary of rates*:
Fert: > 90%
Blastulation: blast/2pn: >50%
Biopsy no result: <2%

*** These rates are specific for the latest laboratory performance, caucasian population, directed and overview by EliteIVF team, using specific equipment and IVF protocols known to enhance performance. Patient ethnic profile, and available equipment may cause variations.**

Fertility Answers Baton Rouge/Lafayette - LA 03/2017 - 03/2018

Director of Laboratory Operations

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- Perform monthly statistical analysis of performance and implement improvement modifications based on data collected;

- **Develop and perform 3 step validation process for every change in technical aspects, assuring best practices, patient protection and best quality of IVF services in every modification necessary;**
- **Provide team's scientific knowledge updates;**
- **Elaborate research study designs, apply, collect and analyze data, and prepare submission for publications.**

Los Angeles Reproductive Laboratories Los Angeles - CA 11/2017 - 03/2018

Director of Laboratory Development and Building

- **Plan, design and develop IVF and andrology laboratories, including equipment, techniques, staffing and accreditation processes;**
- **Oversee building renovation and construction, leading contractor team;**
- **Overview and adapt construction budget;**
- **Maintain technology, quality control and building development rates at necessary workflow;**
- **Recruite, train and supervise lab staffing;**

California Cryobank Los Angeles – CA 08/2015 - 3/2017

Scientific and Technical Laboratory Director of Sperm and Oocyte banks

- **Implement and maintain quality control program for oocyte and sperm banks;**
- **Develop protocols and best practice techniques for cryopreservation of sperm and oocytes;**
- **Provide internal technician training program and quarterly performance analysis - and feedback;**
- **Maintain team scientific knowledge updates;**

- **Develop new research and development department, including elaboration, application and analysis of study designs with pertinent presentation of data to executives;**

Cryopreserved Oocyte Bank specifics:

- **Provide technical training and scientific troubleshooting to affiliated oocyte freezing centers;**
- **Develop technical and scientific relationships with affiliated oocyte thawing clinics, providing real time troubleshooting;**
- **Provide orientation and training for internal and affiliated research and clinical employees;**
- **Collect egg banking performance data from affiliated clinics;**
- **Perform monthly statistical analysis of performance and implement improvement modifications based on data collected;**
- **Develop and perform 3 step validation process for every change in technical aspects, assuring best practices and patient protection and best quality of service in every modification necessary;**

- **2016 main achievements: pregnancy rate for first-year pilot-program = 75% CPR; over 30 centers trained and overseen.**

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Cryopreserved Sperm Bank specifics:

- **Identify gaps in quality of production;**
- **Develop upgraded technical operations system for sperm bank;**
- **Provide scientific background and statistical cost analysis to Operations Department on every recommendation for improvement;**
- **Perform and present statistical analysis of technician performance per branch, and overall in a monthly basis – and pertinent troubleshooting;**

- **Main achievements: Substandard Refund Claims decreased in 2.2 fold; decrease in cost of operations; Reported increase in lab tech job satisfaction.**

Research and Development department:

- **Identify potential partners, create relationships and maintain study designs implemented timely;**
- **Develop and execute study designs for partner biotechnology entities, such as prototype development in gamete and embryo physiopathology and culture, and IVF quality assurance.**

Mexicalli Fertility Center Mexicali – MX 04/2013 –10/2015

Scientific Director

Implement and supervise ART laboratory including performance of all quality control procedures, sample testing, andrology testing, embryology procedures including micromanipulation, cryopreservation and PGD, billing procedures , purchasing management, professional assistance, medical and laboratorial training, plan and overview of hormonal stimulations and advise to outside clinicians on interpretation of results.

Wayne State University Physician Group Southfield - MI 09/2011-03/2014

Embryologist/ Andrologist

Perform quality control analysis, improve ART rates and perform all embryology related duties.
Implementation of cryopreservation program and quality assurance.

IVF Michigan **Ypsilanti, MI** **03/06-02/10**

Lab Supervisor & Embryologist

Supervise ART laboratory including performance of all quality control procedures, sample testing, andrology testing, billing procedures , purchasing management, professional assistance and advise to outside clinicians on interpretation of results.

- Improved IUIS clinical pregnancy rates by implementing standardized policies, procedures and quality control.
- Created and implemented all laboratory polices and procedures from scratch, including andrology procedure manual,
- Completed turnaround of a laboratory which previously failed FDA and COLA inspection to a laboratory which passed COLA inspection in 2007 and received Excellence award in 2009. This required no capital investment or supervision.
- Created and implemented a quality control program according to FDA/CLIA/AAB/ASRM standards
- Developed a system to monitor liquid nitrogen to achieve laboratory capital savings,
- Created and managed sperm cryopreservation/storage billing system,
- Educated medical students/ residents on androloy/embryology procedures

University of Michigan **Ann Arbor, MI** **5/03 – 03/06**

Cryobiology Researcher and Clinical Embryologist

Diagnostic and Therapeutic Andrology, Oocyte collection and IVF, ICSI, Embryo Culture, Cryopreservation of Embryos, Sperm and Oocytes, Laboratory Quality Control. Research on cryopreservation of embryos and oocytes.

- Participated on development and pioneered vitrification of oocytes and embryos technique to achieve 100% survival rates
- Provided full training on vitrification of oocytes to several national and international cryobiology and embryology professionals.

AAB/ABB **St Louis, MS** **06/04- present**

Cryobiology Workshops presenter/medical translations consultant

Performed workshops on diverse methods of vitrification of oocytes and embryos, performed official translation of Embryology and Andrology reviews to South America trainings.

Irvine Scientific **Irvine, CA** **6/03 – present**

Cryobiology Research and Marketing Consultant

Performed research on vitrification of oocytes and embryos, provided multi-language national and international workshops on vitrification including Spain, Belgium, France, Chile, Argentina, Brazil, and many USA cities. Additionally, performed marketing workshop on use of Irvine products.

Biosciences Institute -PUCRS **Porto Alegre, Brazil** **1/98 – 1/01**

Embryology Teacher Assistant and Research Assistant

<u>EDUCATION & CERTIFICATIONS</u>

UFMS – **Brazil**
Post- Grad course: Doctor of Toxicology

East Virginia Medical School- Norfolk- VA
Post grad course: MS Clinical Andrology and Embryology

Catholic University of RS – PUCRS – Porto Alegre, RS Brazil
Bachelor of Biomedical Sciences
H – 12 Teaching Certification

Reproductive Genetic Institute – Chicago, IL
Embryo Biopsy and PGD Training

Certified Embryologist and Andrologist at technical supervisor level by AAB since 2007.
AAB/ABB, ESHRE and ASRM/ SRBT member.

AWARDS

2018: AAB/ABB Meeting CRB Scholarship Award
2017: AAB/ABB Meeting CRB Scholarship Award
2011: AAB/ABB David Bierbaum Scholarship Award;
2011: Premio da iniciativa privada em excelencia na area da educacao. Porto Alegre RS- BR

LANGUAGE SKILLS
English: Fluent;
Portuguese: Fluent; Native Language
Italian: Fluent: Native language.
Spanish: Conversational, fluent reader
French: Conversational, fluent reader

PUBLICATIONS

- Industry guidelines on safety of reproductive tissue cryobanking. 2018, Embryology, V 218, 1. AAB online publications.

- Gomes C, ***Silva C***, Acevedo NA, Serafini P, Baracat E, Smith GD. Influence of vitrification on mouse metaphase II oocyte spindle dynamics and chromatin alignment. Fert and Steril (2008).
- Davis, D. ***Silva, C***. Hiner M. and Smith G. Assisted Reproductive Technology – lab Review. Clinical Reproductive Medicine and Surgery. Falcone & Hurd. Elsevier, 2005
- Smith, G.D. & ***E Silva, C.A.S***. Developmental Consequences of Cryopreservation of Mammalian Oocytes and Embryos. RMB on line Volume 9, No 2 August 2004.

ABSTRACTS

- Main troubleshooting root causes in IVF and cause analysis: an overview of 150 cases 2016 PUCRS annual international meeting.

- Zona Pelucida Modifications and Fertilization Following Metaphase II Oocyte Vitrification and Warming. 2005 ASRM meeting - Montreal, Canada.
- Influence of Vitrification on mouse and Metaphase II spindle dynamics, spindle morphology and chromatin alignment. 2004 ASRM meeting - Philadelphia, USA.
- Vitrification of Methaphase II Oocytes: A Prelude to Successful Preervation of Fertility – 2004 AAB annual meeting - Las Vegas, USA
- Vitrification of Mouse Methaphase II Oocytes: A prelude to successful Preservation of Reproductive Capacity in Female Patients – University of Michigan Ob Gyn Symposium - 2003 Ann Arbor, USA.

- Embryo morphology as a predictor of pregnancy success: time lapse of first divisions in association with Gardmer's grading system. 2001 PUCRS biomedical scientific meeting.
- Timing of first embryonic cleavages: a prediction of embryo quality. 2000 ESHRE

INSTRUCTOR FOR PROFESSIONAL ACTIVITIES

2018: ASRM Roundtable program discussion: Advances on cryopreservation of oocytes and cryobaning troubleshooting: how to guarantee success and safety of reproductive tissue.

2018: AAB/ ABB meeting: Moderator

2018: AAB/ ABB CRB annual meeting: Roundtable Workshop presentation: Guaranteed Success on Cryopreservation of Oocytes and banking: Why my D3 are not becoming clinical pregnancies.

2017 AAB/ ABB CRB annual meeting: Roundtable Workshop presentation: Techniques for a more efficient cryopreservation of oocytes program.

- 2008: Hands on workshop on vitrification of oocytes: Training for Clinical Embroyologists Rush Medical Chicago, IL
- 2008: Hands on workshop on vitrification of oocytes and embryos – Barcelona, Spain
- 2007: Hands on workshop on vitrification of oocytes: Training for Clinical Embroyologists Rush Medical Chicago, IL
- 2007: Hands on workshop on cryopreservation techniques: 1st Encounter for Embroylogists – Porto Alegre, Brazil.
- 2005: AAB Workshops on Vitrification of Oocytes: Training for Clinical Embroyologists – Irvine, USA
- 2005: Hands on Workshops on Vitrification of Oocytes: Training for Clinical Embroyologist – Irvine, USA
- 2004: Hands on Workshops on Vitrification of Oocytes: Training for Clinical Embroyologists – San Francisco, San Antonio, Chicago, Ft. Lauderdale, Madrid, Brussels, Paris, Santiago de Chile, Buenos Aires, Sao Paulo, Caracas,
- 2001: Manipulation and Diagnosis of Embryos: Techniques and Ethical Issues. Pontificy Catholic University of Rio Grande do Sul, Brazil.
- 2001: Symposium: Participation with Oral Exposition: Maniuplation of Human Embryos and Ethical issues. Pontificy Catholic University of Rio Grande do Sul, Brazil.
- 2001: Classes of In VitroFertilization on Medical and Biological Sciences. Fisiotherapy and Nursing School as invited specialized professional. Pontificy Catholic University of Rio Grande do Sul, Brazil.
- 2000: Symposium Genetic Manipulation of Horses. Annual meeting of crioulos horse farms of Rio Grande do Sul, Brazil.

TEACHING EXPERIENCE:

- 1998 – 2001 : Embryology, Histology, Advanced Genetics teacher's assistant – PUCRS Medical School and Biosciences Departments - Brazil